THE
AMERICAN REVIEW OF TUBERCULOSIS
ABSTRACTS OF TUBERCULOSIS

VOLUME XI JUNE, 1925 ABST. NO. 4

Action of War Gases on Respiratory Tract and Respiration.—*1: General intoxicants:* These may be briefly dismissed as being scarcely employed at all in warfare. Such are hydrocyanic acid and carbon monoxide. The latter kills, not by any special propensity for the bulbar centres, as long believed, but by preventing tissue respiration by substituting itself for oxygen in the hemoglobin molecule. *2: Suffocants:* This includes chlorine, or phosgene diphosgene, and certain lachrymogens. These gases irritate the nerve terminals of the trigeminal and glossopharyngeal, and reflexly check expiration. They penetrate deeply into the respiratory passages without undergoing much condensation until the final ramifications of the pulmonary tree, where they affect the sensory terminals of the pneumogastric; this in turn arouses a polypneic reflex antagonistic to the first, and the result is a sense of suffocation combined with retrosternal and thoracic pain. Several days later, especially in the case of chlorine, there develops a laryngitis and tracheobronchitis, more or less difficult to cure. The damage to the fragile alveolarepithelium, on the other hand, persists, and attains considerable gravity at the end of several hours. The suffocants hydrolyze rapidly in the alveolar walls, forming nascent acids, HCl, HBr, or HI, which produce burns and edema. This pulmonary edema is the most formidable complication of intoxication by suffocants. It sometimes develops in a fulminating manner. Treated properly, it may disappear in several days, but the pulmonary lesions may become secondarily infected, and bronchopneumonia or bronchial suppurations ensue. Even in the mild cases functional troubles may appear, such as attacks of rapid superficial respiration and bronchial spasm similar to asthma. These troubles interfere with aeration, lower the oxygen tension of arterial blood, and produce anoxemia. This condition is capable of setting up all sorts of functional disturbances in various organs. *3: Vesicants:* Among the chief of these are yperite or sulphide of dichlorethyl and, in some measure, the arsines. The action is exerted chiefly on the upper respiratory tract and bronchi. Yperite has a low vapor tension which allows it to condense on the first portions of the respiratory tree and hydrolyzes slowly. It also has an affinity for the lipoids, which explains the production of burns in thick and resistant tissues. On contact with water it yields HCl and $S(C_2H_4OH)_2$, or dihydroxyethylsulphide. The hydrochloric acid provokes edema and local vasodilatation after a latent period of several hours to several days. Thus are set up rhinitis, laryngitis, bronchitis and bronchopneumonias, all of which favor anoxemia. Both lungs may be blocked. Septic infection may be superimposed, as the burns furnish a ready soil for saprophytes, and the superadded infectious element aggravates the already precarious situation. *4: Lachrymogens:* (Bromine, benzyl iodide, etc.) These likewise act as suffocants. *5: Sternutators:* (Liquid and solid arsines). These provoke repeated sneezes by irritation of the nasal mucosa. Frequently there is also a congestion of the frontal sinuses accompanied by pain. Inhalation of the arsines also produces symptoms like those due to yperite. *Respiratory sequellae:* Many gas patients present few or no sequellae. Others are subject to recurrent attacks of congestive edema, pulmonary emphysema with or without asthma, pseudotuberculous sclerosis, and lung abscess; also chronic bronchitis attacks, or even foci of bronchopneumonia. Hilar and peribronchial adenopathy may develop, and functional respiratory disturbances, many of which are traceable to or result in

defective oxygenation of the blood. The anoxemias may be divided into: 1. Anemic anoxemia in which the oxyhemoglobin is diminished. 2. Hypercapnic anoxemia, characterized by both oxygen deficit and excess of CO_2 in the arterial blood. This type occurs especially with stenosing bronchitis, bronchopneumonia and emphysema. It is associated with blue cyanosis, due to capillary dilatation, with venous engorgement and engagement of the right heart. 3. Acapnic anoxemia, when the CO_2 tension of the arterial blood is lowered. This form is the gravest of all, since respiration is superficial, the circulation is slowed, and a vicious circle established. This type is met with in mountain sickness, carbon monoxide poisoning, and poisoning by phosgene and chlorine, especially the latter. The myocardium and nervous centres are affected. The anoxemia results in diminished capacity for effort, and often in paralysis or neuritis, a state of hypersensitiveness and adynamia, with irritable heart, recalling severe neurasthenia. "Irritable heart" has been especially carefully studied by L. Dautrebande. The subjective symptoms are: short respiration, a sense of thoracic constriction, precordial pains, palpitation, tendency to vertigo and syncope, and ease of tire. The objective symptoms are exaggerated apex impulse, tachycardia, especially on lying down, and frequently a murmur, variously located. Functional symptoms are: emotion and exertion tachydardia, shortened systole, rapid superficial respiration, and acapnic anoxemia. The symptoms appear to be due to deficient oxygenation of the myocardium, impaired circulation, and hypotonicity of the respiratory centre. There is a general lack of nervous tone, as seen in the neurasthenic, and neurasthenic symptoms often coexist. Dautrebande and the author, from extensive experience with gassed cases since 1918, have concluded that to be related to the action of the gas these sequellae must follow shortly after the intoxication. Not all of the gassed have sequellae. Many return to normal health and show no clinical, radiological or functional abnormalities. Many of the same anoxemic and neurasthenic disturbances are to be found among those never exposed to war gases. Constitutional defects, epidemics of dysentery and grippe, repeated war emotions, or difficulties of existence during peace time have much more to do with these supposed sequellae of gassing. *Relations with pulmonary tuberculosis:* Physicians are generally in accord in the opinion that the proportion of gassed cases later becoming tuberculous is exceedingly small. It is true that repeated or prolonged fatigue, diseases greatly reducing the general vitality (grippe, dysentery), successive respiratory infections, all of which were frequent in the army, favor to a certain extent pulmonary localizations and outbreaks. Likewise, the difficulties of life after the war, poor hygienic conditions, and insufficient nutrition explain the recrudescence of many cases. Such cases of tuberculosis as may be said to have relation to gassing or its sequellae are predominantly of the fibrous sclerosing types. *Treatment:* Bleeding and continuous oxygen inhalations have proved most effective in acute pulmonary edema and certain forms of bronchopneumonia. Fresh air and rest, physical and respiratory reëducation are valuable for the later sequellae of neurasthenia and irritable heart. The results at Grande Bretagne show that these patients are more amenable to cure than is frequently supposed.—*L'action des gaz de combat sur l'appareil respiratoire et la respiration, P. Spehl, Rev. Belge d. l. Tuberc., July, 1924, no. 7, 222.*—*(A. P.)*

Experimental Study of Deep Respiration.—The work of Haldane, Barcroft, Krogh and Benedict has clarified our conceptions of respiratory physiology and led to further researches of much practical importance. *Respiratory physiology:* The function of respiration may be divided into three stages, the pulmonary, the circulatory, and the tissular. *1: Pulmonary phase:* With each respiratory movement about 500 cc. of air circulates. With a deep inspiration about 1500 cc. more are added; also a vigorous expulsive effort drives out about the same amount, and there is a volume of about 1000 cc. residual air which cannot be expelled, giving an average total pulmonary capacity of 4000 to 4500 cc. The air which is found in the depths of the alveoli contains about 5.6 per cent CO_2, while that which issues from the respiratory passages contains only 3 to 3.5 per cent CO_2. Haldane has shown that only a portion of the inspired air penetrates to the alveoli, the remainder only going as far as the larger bronchi. The space occupied by this portion of the air, which does not truly participate in respiration, he has called the "dead space." Thus it happens that the expired air is really a mixture of alveolar air with air from the dead space, which contains very little CO_2. The English school has also shown that the composition of the expired air varies with the quantity which penetrates the lung, production of CO_2 by the tissues, the pure air contained in the dead space, and the frequency of respiration. Respiration is generally more effective with deep than with

shallow breathing, as will be seen by analysis of the expired air. According to Haldane's law, "the alveolar air of a healthy subject at rest is constant in its composition" (about 5.6 per cent CO_2). As we know that gases act only by reason of their partial pressure, it follows that the alveolar air of a healthy subject at rest has a partial pressure of CO_2 of about 40 mm. mercury. If, however, there is some obstacle to alveolar expansion, or to penetration of air within the lung, there is a stagnation of air, which results in an accumulation of CO_2 and a diminution of oxygen in the alveolus. Dautrebande has shown this to be the case in persons with extensive tuberculous lesions, whose alveolar air contains 6 per cent CO_2. A forced expiration will contain a higher percentage of CO_2 than normal expired air, because it contains more of the air in contact with pulmonary epithelium. Repeated deep expirations should lower the CO_2 tension of the alveolar air. *2: Circulatory phase:* The inspired air in the pulmonary alveoli comes in contact with a large blood surface which is at its maximum at the height of inspiration, due to the expansion of the lung and thoracic aspiration of venous blood, which becomes charged in the lungs with oxyhemoglobin. The acidity of the oxyhemoglobin forces alkaline carbonates and bicarbonates to give up their alkaline radicles and release CO_2. The expulsion of the carbon dioxide depends first on the combined oxygen in the blood, also on the richness of the plasma in carbonates and bicarbonates, and finally on expiratory forces (pulmonary elasticity and respiratory musculature). When the oxyhemoglobin is carried to the tissues it abandons its oxygen, becomes less acid and liberates the excess alkaline radicles borrowed in the lung. The CO_2 from the tissues at once combines with the liberated alkali into carbonates and bicarbonates. It is, therefore, the alkaline reserve of the plasma which permits the transporation of carbon dioxide. On its relations with the free CO_2 will depend the limits of reaction of the blood established by Henderson. Thus, if the bicarbonates diminish, carbon dioxide will be eliminated up to the point of exhaustion of the alkaline reserve, when the blood will become acid and other organs will be called upon to neutralize the excess acidity. This excess acidity in turn produces a hyperventilation by a bulbar reflex, in order to wash the blood of its CO_2, and an increase in ammoniacal secretion by the liver and kidneys. In the course of certain affections, such as diabetes and nephritis, this course of events occurs. If, on the contrary, the CO_2 saturation in the blood diminishes, as after prolonged hyperventilation, there is produced an increase in the alkaline reserve, and the blood, to maintain its proper reaction, must eliminate alkali in the form of phosphates. Thus the body faces two vital necessities, namely, to eliminate organic acids, and to maintain a reserve of alkaline metals and earths to serve as vehicles for eliminating the acids. *3: Tissular phase:* The gaseous exchanges to and from the capillaries follow the physical laws governing exchange through permeable membranes. Not all the oxygen absorbed goes to produce dioxide; there are also subproducts, such as urea, sulphates and water. The relation between the volume of CO_2 eliminated and that of oxygen absorbed measures the intensity of combustion, and is termed the *respiratory quotient* (*R. Q.*) This is ordinarily 1 for carbohydrates, 0.8 for fats and 0.75 for proteins. The nervous system presides over the respiratory movements, through the intermediation of a bulbar spinal centre, which Haldane has shown is sensitive to an increase of 0.02 per cent of CO_2 in the blood. The expiratory phase is passive, the lung recoiling due to its elasticity, but inspiration is inaugurated by stimuli from the brain, bulbar centre or blood. When the lung is fully distended, impulses passing by way of the vagus to the bulbar centre check further inspiration. During deep respiration there is a maximum lung ventilation, which washes out the CO_2 from the alveolar air and lowers the tension of this gas in the blood and tissues. The blood then tends to become alkaline. If its reaction becomes acid, as after intense muscular exercise, it may be seen that deep respirations greatly help to combat this excess acidity. *Experimental studies:* The oxygen and carbon dioxide content of both expired air and alveolar air were determined at rest with normal breathing, at rest with deep breathing, during ordinary breathing after running 1500 metres, and after deep breathing following running. The subjects were military cadets in training. The apparatus used was Amar's, together with Laulanie's endiometer. All readings were reduced to 0°C. and 760 mm. mercury barometric pressure. The following were determined or calculated: (1) curve of pulmonary ventilation over a ten-minute period, (2) percentage composition of expired air and of alveolar air, (3) value of the "dead space" and (4) the "effective pulmonary ventilation." *Pulmonary ventilation:* The respiratory rate is constant at rest, raised by exercise, and returns to normal in three to five minutes. Deep breathing increases the spirometric readings about 50 per cent and doubles the CO_2 elimination. It also raises the *R. Q.* temporarily. Running increases pulmonary

ventilation over 100 per cent, triples the CO_2 elimination and oxygen absorption rate, and further raises the *R. Q.* These figures subside after two minutes. Deep breathing after running increases ventilation 120 per cent, quintuples CO_2 elimination, nearly quadruples oxygen absorption and raises the *R. Q.* to almost 1. *Alveolar ventilation:* After deep breathing while at rest, the CO_2 tension of the alveolar air is lowered about 20 per cent, and that of oxygen raised about 1 per cent. Running increases the CO_2 tension and lowers the oxygen tension. Deep breathing after running diminishes the heightened CO_2 tension and greatly increases that of oxygen. Hyperventilation, however, while washing away the CO_2 from the alveoli, does not greatly affect oxygen absorption, because of the saturation limit of oxyhemoglobin. The excess oxygen inspired merely returns with the expired air after passing through the pulmonary tree, and gives the latter a higher oxygen content than the alveolar air. The respiratory rate does not increase so much if a series of deep breaths are taken after running because these wash out much of the excess CO_2. *The dead space:* This can be very simply calculated if one knows the quantity of the tidal air and the CO_2 content of this air and of the alveolar air. If the figure for the former is 3 per cent, for the latter 4.4 per cent, and the quantity of tidal air 752 cc., we have $\frac{0.752 \times 3}{4.4} = 501$ cc. alveolar air, which when subtracted leaves 251 cc. dead space. One can then calculate the *effective respiration* per minute, knowing the respiratory rate. The results of these experiments indicate the value of respiratory training and rational use of breathing exercises. Deep breathing is shown to diminish the work of compensation otherwise imposed on other organs, including the liver and kidneys, to maintain the proper reaction of the blood.—*Analyses expérimentales de la respiration profonde, A. Govaerts, Rev. Belge d. l. Tuberc., July, 1924, no. 7, 211.*—(*A. P.*)

Determination of Chest Expansion.—The thoracometer is an instrument for determining the difference in expansion of the two sides of the upper chest in pulmonary thberculosis. It is built after the plan of the original caliper, with special features attached to the free ends. One arm is longer than the other, and has attached to it a pad of the ball and socket type, permitting free movement and conformity to the surface of the body. The other and shorter arm has attached to it a measuring device, composed of a barrel with a movable rod passing through, and controlled by a coil spring. The points of operation are the fourth or fifth dorsal spine and second rib, about two inches from the margin of the sternum.—*An Instrument to Determine the Difference in Expansion of the Two Sides of the Upper Chest in Pulmonary Tuberculosis, I. R. Wagner, J. Am. M. Ass., August 23, 1924, lxxxiii, 613.*—(*B. T. McM.*)

Motor Innervation of Diaphragm.—Observations, 136 days after section of the phrenic nerve, indicated that the motor innervation of the diaphragm was entirely due to this nerve, a complete hemiatrophy being obtained. If the diaphragm were supplied by another nerve this would be partly prevented, and a compensatory hypertrophy might even be expected. Contractions upon electric stimulation were strictly unilateral. Electric stimulation of the lower intercostals, along the back muscles and in the spinal canal, revealed in dogs that they possessed no motor branches to the diaphragm. Stimulation of the vagus also caused no contraction of the diaphragm. Faradic stimulation of the phrenic nerve gave violent contractions of the entire half of the diaphragm. Clinical observations also establish the phrenic innervation of the diaphragm. Autopsy findings in cases of phrenicotomy also bear this out, and all data would indicate a strict motor innervation of the diaphragm by the phrenic nerve alone.—*Beitrag zur Frage der motorischen Innervation des Zwerchfelles, K. Schlaepfer, Beitr. z. Klin. d. Tuberk., September, 1923, lvi, 261.*—(*H. J. C.*)

Lung Fats and Calcium Fixation.—Having shown that the lung fats exert a favorable influence on growth due to vitamine-A which they store up in sufficient quantity, the existence in these fats of antirachitic vitamines which help the body to fix calcium is insisted on. Submitted to regimen 85 of Pappenheimer, young rats are not slow to develop rickets. If the butter of the regimen is replaced by fats extracted from a dog's lung, the calcification of the skeleton proceeds normally, as shown by histological examination of the costochondral zone.—*Action des graisses du poumon sur la fixation du calcium, H. Roger, L. Binet and M. Vagliano, Société de Biologie, July, 1924, reported in Presse Méd., July 9, 1924, no. 55, 582.*—(*B. T. McM.*)

Kidney Function and Water Balance in Pulmonary Tuberculosis.—The determination of the water-excretion quotient, that is, the ratio between the daily intake and output of water in pulmonary tuberculosis led to the following results: Values of 90 per

cent and over were found, in the main, in good cases, while in exudative forms lower values, for instance, 70 per cent, were found; in other words, good forms of the disease are associated with better excretion than are the severe forms. No relation between this and the temperature or body weight was noted. Since the skin can be excluded as an excretory organ for the excess fluid it can be assumed that the latter is excreted with the expired air. The more extensive and severe is the disease process in the lung the greater are the oxidation processes, the more rapid the respiration and the greater the water excretion by this route. Kidney-function tests revealed an almost normal urine content, and the concentration did not vary much from normal; in a few severe cases it was not normal. Greater variations occurred in the fluid excretion of the first four hours; a good excess was excreted in the favorable cases, while in severe cases excretion was diminished. Simultaneous blood-pressure determinations revealed that an arterial hypotonia was of no significance, and the temperature was without significance. No pathological kidney findings existed; therefore extrarenal factors must be sought to explain this condition, and especially must the osmotic pressure of the plasma proteins be considered (an increase causes inhibition and decrease a diuresis). This pressure is again dependent upon the dispersion of the plasma proteins, which is greater according as the content in low disperse protein fractions is higher. The lowest disperse protein fraction is fibrinogen. As is determinable by the erythrocyte sedimentation rate, the fibrinogen content is largest in acute and progressive forms of disease, and in these cases the osmotic pressure and water-binding power of the plasma is increased most, and the diuresis is diminished. The condition of the tuberculous process can be prognostically determined according to the kidney-function test.—*Über Nierenfunktion und Wasserhaushalt bei Lungentuberkulose, A. V. Fresch, Beitr. z. Klin. d. Tuberk., June, 1923, lv, 1.*—(*H. J. C.*)

Blood-Platelet Counts in Tuberculosis.—The relation of blood-platelets to microbial infection has been the subject of much study. That a diminution of their number is associated with lowering of resistance to infection has been proved by several investigations. In the human subject the author has observed a thrombopenia during acute infection. However, in pulmonary tuberculosis—a chronic disease—the blood picture was very different, the tendency being to a thrombocytosis. The technique is described only in part, reference being made to a previous paper. In a series of normal subjects the count was found to vary from 250,000 to 380,000 per cmm. Sixty-five cases of pulmonary tuberculosis gave counts ranging from normal to 1,000,000 per cmm. All observations were made at an altitude of 5000 feet, where the normal red-cell count is in the region of 6,500,000 per cmm. In tuberculosis cases it was found, as a rule, that the more serious the clinical condition the greater the degree of thrombocytosis. Repeated counts showed that a change in the direction of the normal coincided with an improvement in the clinical condition, whereas a movement in the opposite direction or the persistence of a high count was associated with a progression of the disease. On the other hand, the maintenance of a normal count pointed to stability. It appears that there exists an inverse relation between thrombocytosis and the subject's resistance to the disease; and it is suggested that the platelet count may afford a means of measuring that somewhat indefinite entity which is the basis of prognosis.—*Blood-Plate Counts in Pulmonary Tuberculosis, R. G. Bannerman, Lancet, September 20, 1924, ccvii, 593.*—(*J. S. W.*)

Carbon-Dioxide Combining Power in Tuberculosis.—In advanced pulmonary tuberculosis ventilation is about twice the normal, and a much lower percentage of CO_2 is present in the expired air. The total amount, however, is greater in the tuberculous than in the normal. The carbon dioxide combining power of blood plasma was ascertained in several groups of tuberculous individuals varying from ambulatory to very far advanced types. Surprisingly uniform results were obtained: the far advanced had a combining power of 61.3 (average); the moderately advanced, 64.4; early cases, 57.6; ambulatory, 63.4; and controls, 61.2. The influence of fever was taken into consideration. In 6 cases with temperature above 100°F., the average combining power was 63.5; in 26 cases with temperature lower than this the average was over 61.7. Although no evidence of acidosis was thus shown, there was a highly acid urine and this, plus the CO_2 elimination through expired air, suggests the continuance of alkali therapy.—*Carbon Dioxide Combining Power of Blood Plasma in Pulmonary Tuberculosis, F. P. Miller, California and Western Med., June, 1924, xxii, 273.*—(*H. S. W.*)

Tuberculosis in Man and Animals.—In studying tuberculosis in many kinds of animals the difference in appearance of the lesions in different species was noted early. Tuberculosis in some species would not,

on mere inspection, be recognizable as such by anyone who was familiar with the disease only as it occurs in man. For example, the nodular masses or "grapes" in the ox; the white nodular-like marbles in the spleen of the pig; the round, bile-stained, necrotic masses in the liver and spleen of the fowl; the projecting hemispherical nodules on the surface of the rabbit's kidney; the enormous piebald spleen in the guinea pig which looks like castile soap; and the barely discernible lesions in the rat are mentioned. Two points are to be considered when attempting to explain these peculiarities: the anatomic structure of the organ in question, and its biological response to the infective agent. There exists in the ox, developed to an extent probably seen in no other species, a system of little villus processes which arise from the serous membranes lining its cavities and covering some of its organs. These are presumably normally concerned with the drainage of these cavities, but in tuberculosis they may take up the bacilli and develop into tubercles and tuberculous nodules. It is on the lungs that these processes reach their greatest development. There they appear as a lace-like fringe along the margins of the lobes, and as tags arising from their surfaces. The peculiar character of these lesions of tuberculosis as seen in the ox is believed to be due to their special anatomic structure. The disease consists of two processes, growth and destruction. In the ox, growth preponderates with such results as are noted above, but in man, as a rule, destruction prevails over growth and we find, instead of tumors, ulcers, abscesses, or cavities. Such differences are probably caused by inequalities in sensitiveness to the endotoxin of the bacillus, which acts upon the connective tissue of some animals as a stimulus to growth, and upon others as a destructive agent. But there is a third class, upon which the endotoxin appears to exert but little influence of either kind. Such insensitiveness is shown in an extreme degree by the rat. An injection of tubercle bacilli causes no obvious reaction in this animal. But while the rat appears to take no notice of its invaders, little by little they increase in numbers and eventually they destroy it. Although, on examination, very little change is seen in the appearance of the organs, microscopically they are found to contain an incredible number of bacilli. If the organs are considered which contract tuberculosis as a rule from the blood-stream only, it is noted that in each species there is a peculiar and characteristic distribution of the lesions. Examination of one guinea pig after another, dead of a subcutaneous injection of tubercle bacilli, shows the same distribution of lesions in all, but on studying tuberculous animals of different species it is found that the organs which are constantly affected in one species escape in another. In the rabbit, after subcutaneous or intraperitoneal injection, or even after ingestion of tubercle bacilli, the lungs and the kidneys bear the brunt of the disease while the spleen is less severely affected, and the liver rarely. On the contrary in the guinea pig, after similar means of infection, it is preëminently the liver and spleen which suffer, the lungs showing a remarkable resistance and the kidneys usually escaping entirely. Has each animal its special weak points? The guinea pig seems to be weak in the arrangements for draining the pleural cavity of superfluous fluid; for this animal, after various kinds of infection, often succumbs to pleural effusion and consequent collapse of the lung. But, although such or similar points of weakness do exist, on the whole it is not some weakness of a given system or organ to resist infections or toxins, but rather an incapacity in such a system successfully to resist the attack of one particular pathogenic agent, which accounts for the vulnerability. Thus the cow's udder is very liable to be damaged by the tubercle bacillus, but is not otherwise a particularly vulnerable organ; and in man the salivary glands, which are the chief seat of selection in mumps, enjoy a remarkable immunity from other infections. Speaking generally, there is probably no system in the body which suffers more often from tuberculosis than the lymph nodes. The purpose of these structures is to purify the lymph, and to filter out any bacteria present, and to attempt to destroy them. The lymph nodes are especially liable to tubercle, not because they are deficient in resisting power, but because their job is to deal with dangerous agents. In birds they do not exist; and these creatures must resist disease without their aid. In the rabbit where they are well-developed, they do not play so conspicuous a part as in the guinea pig and ox. In man, the lymph nodes are not equally liable to develop tubercle at different periods of life. Next to the lymph nodes the lungs are preëminently the commonest seat of tuberculosis in nearly all animals. So frequent is the form of the disease that the lungs are commonly regarded as offering a more favorable soil for the growth of tubercle bacilli than any other organ. This is not the case, however. Tubercle bacilli will grow and produce lesions in any organ or tissue, even the muscles themselves, if they get planted there. The lungs owe their great liability to be chosen as the principal seat of tuberculous disease to their unique anatomic position.

Not only do they receive directly the bacilli which are carried to them in the inspired air; but to them, before any other organ, come the bacilli which, after entering the body through any of its portals, have by some means won their way into the blood. Thus, not only is air-borne tubercle almost always a disease primarily of the lungs, but blood-borne tubercle bacilli are in a better position to attack these organs than any other. The relative freedom from serious pulmonary disease shown by young children with bronchial-node tuberculosis is explained as being due to the lowered capacity of the child's lungs for detaining bacilli. Why are certain organs attacked more frequently in one species than in another? Tubercle of the mammary gland is unknown in guinea pigs, yet is by no means rare in the rabbit. Tuberculosis of the human breast is uncommon, whereas the frequency of this infection in the cow's udder is notorious. In man tuberculous meningitis causes 8 per cent of the deaths attributed to tuberculosis at all ages, whereas in cattle tuberculosis of the central nervous system is found in only 0.56 per cent. With respect to these organs, whose liability to tubercle exceeds in certain animal species that of similar organs in all other species, it is emphasized that they all have this in common, namely, that they have more work to do than the corresponding organs of other animals. Also, in seeking the cause of this increased liability to tubercle, the possibility must not be ignored that overwork, with its accompanying fatigue, and accumulating of waste products, may be an important factor. It has been stated that the liability of organs of great functional activity to hematogenous tubercle is due to the fact of their receiving large supplies of blood. This explanation is inadequate. The kidneys of the guinea pig probably receive as much blood as the neighboring spleen, yet the susceptibility of the two organs is widely different. It has been suggested that susceptibility to tubercle in any organ depends largely on whether the tubercle bacilli, when brought to it by the blood, are detained in the organ or allowed to pass on their way. It is known that tubercle bacilli consist largely of some waxy or fatty substances, and it is suggested that this substance exerts a chemotactic influence identical with that of some food particles, which are greatly sought after by certain organs and not by others, and by a given organ to a greater extent in one species than in another. Susceptibility to tubercle, then, depends, according to this view, on the strength of the demand made by the organ or system for some particular kind of fatty food, which food happens to resemble in its chemical affinities the fatty part of the tubercle bacillus. The hypothesis may be an explanation of the fact so tragically demonstrated during and immediately after the war, especially in Central Europe, that a shortage of fats is accompanied by a great increase in the death-rate from tuberculosis. —*Tuberculosis in Man and Domesticated Animals. The Relative Susceptibility to the Disease of Their Various Organs, L. Cobbett, Tubercle, October, 1924, vi, 1*—(*J. S. W.*)

Mild Generalized Tuberculosis of Adults.—The mild generalized tuberculosis of the adult, secondary tuberculosis, is to be strictly differentiated from chronic pulmonary tuberculosis. It is always favorable, but the case is more in danger of developing a chronic pulmonary tuberculosis than normal. Diagnosis is not always possible and can be made only by correlating anatomic, bacteriological and clinical findings and local and general symptoms. The outcome of the tuberculin test or specific treatment is only of presumptive value. Roentgen examination is unreliable and will often reveal the picture of hematogenous dissemination in the lungs.—*Die milde generalisierte Tuberkulose des Erwachsenen, E. Fraenkel, Ztschr. f. Tuberk., May, 1924, xl, 181.*—(*H. J. C.*)

Pleural Annular Shadows.—The literature on roentgenographic annular shadows and related phenomena is reviewed. The contention that all such shadows represent cavities is disputed, and criteria for distinguishing cavities and pleural formations are presented. The position taken by some workers that small pneumothoraces are frequent in pulmonary tuberculosis is questioned. Evidence is given in an attempt to show that the shadows are due most often to simple pleuritic changes, and in an addendum, the clinical report of Hebert and autopsy studies of de Jong and Pestel and of Ramos-Casellas are cited as direct proof of this. *Conclusions:* There is good evidence that the roentgenographic annular shadow, as an accompaniment of pulmonary tuberculosis is a reality. Exact proof of the significance of these shadows is lacking, but from a critical consideration of their attributes it appears that most of them represent simple limited pleurisies not differing fundamentally from the usual chronic or subacute tuberculous inflammations. The lesion is sometimes associated with separation of the pleural membranes and the resulting interstice may contain fluid. A pleural interstice may be created probably by one or more of a number of forces operating inside

or outside the lung, and there is no proof that its demonstration is an invariable, or even a usual, criterion of perforation of a tuberculous focus through the pleura. The true incidence of perforation of the tuberculous lung into a small intact pocket of pleural adhesions is an open question. Autopsic examination, after the lesions have been localized by the roentgenograph and with the special conditions in mind, is required to throw light on a problem the clinical significance of which is important. Clinically it has been established that these annular shadows develop and increase in size as accompaniments of active disease in the subjacent lung, and that they contract and fade as this activity subsides.—*The Significance of Roentgenographic Pleural Annular Shadows, Present Conceptions, J. B. Amberson, Jr., Tubercle, August, 1924, v, 534.*—(*J. B. A.*)

Significance of Cavities in Pulmonary Tuberculosis.—Cavities are almost always found in rapid, severe, exudative pulmonary tuberculosis, that often terminates a few months after the first appearance of clinical symptoms. In such cases the lethal outcome is not to be associated with the cavity formation. Cavity is to be viewed more as an evidence of severe destruction of the lung and may favor the spread of the disease, and hasten deaths, but it does not occasion the latter. Cases are seen that live many years in spite of their cavities, and in good physical condition; 13 cavity cases lived 4 to 11 years after discharge from the sanatorium, were capable of work during the greater part of the time and became free from bacilli. The sanatorium results with cavity cases are not entirely unsatisfactory, and do not justify the view expressed by Graeff that they should be excluded from sanatorium treatment.—*Untersuchungen am klinischen Material über die Bedeutung der Kaverne für die Lungentuberkulose, K. Lydtin, Zeitschr. f. Tuberk., October, 1923, xxxix, 1.*—(*H. J. C.*)

Pulmonary Scars.—The lungs of 200 nontuberculous individuals over 20 years of age were studied. Of these 9 per cent had scars and connective-tissue foci in one or more lobes. In 93 per cent of the cases the scars were associated with dense pleural adhesions, indicating the existence of earlier inflammatory conditions of the lungs. As a result of these scars there develop bronchiectatic and gangrenous pulmonary conditions.—*Die bindegewebigen Verdichtungsherde in den Lunge ihr Vorkommen und ihre Folgezustände, A. Beckmann, Virchow's Arch. f. pathol. Anat., 1923, ccxliv, 84.*—(*H. J. C.*)

Healing of Miliary Tuberculosis.—There are described forms of slowly progressing, chronic miliary tuberculosis, in which the prognosis was not especially unfavorable. More severe forms also improve unexpectedly and terminate in clinical healing. A case of the latter type is presented in which clinical healing required seven months; this was followed by a relapse and death from tuberculous meningitis. The diagnosis of miliary tuberculosis of the lungs was made by the symptoms and roentgenological findings. The anatomic diagnosis was *Tuberculosis pulmonis miliaris sanata* and *Meningitis basilaris tuberculosa.—Über die Möglichkeit der Heilung der Miliartuberkulose, T. v. Kern and B. Tohan, Beitr. z. Klin. d. Tuberk., June, 1923, lvi, 41.*—(*H. J. C.*)

Associated Infections in Pulmonary Tuberculosis.—Caseating extensions and pericaseous pulmonary reactions are attributable solely to the tubercle bacillus. All these transformations go on without the presence of polynuclears. Staining technique permits us to demonstrate the tubercle bacilli everywhere in these lesions, even to the placques of alveolitis. Thus, the miliary granulation, the tuberculous nodule, the massive caseous pneumonia, the macrophagic reaction and caseation, are all the work of the tubercle bacillus; likewise the acute pericaseous inflammatory reactions. When caseous foci liquefy, the problem becomes more difficult. In such a suppurating caseous mass one can often find, besides tubercle bacilli and polynuclears, other microörganisms, especially cocci. Sometimes these latter are very numerous. What is their rôle? It seems most likely that they are late arrivals at the time when or after bronchial communication with the tuberculous suppurating foci is established. These extraneous invaders are never found in the caseating masses themselves, nor in the surrounding inflammatory zones. They may, however, set up a secondary bronchitis, in which case the inflamed mucosa shows their presence with polynuclear cells, and without tubercle bacilli. Such subsidiary lesions, however, have no effects on the course of the tuberculous process itself.—*Bacilles tuberculeux et microbes associées dans l'histo-pathologie de la tuberculose pulmonaire, M. Letulle and P. Halbron, V^e^ Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 373.*—(*A. P.*)

Associated Infections in Pulmonary Tuberculosis.—These were carried out at the Military Hospital of St. Genis-Laval (Rhone). They led to a rejection of the doctrine of secondary infections in pul-

monary tuberculosis, a doctrine which harks back to the dualistic conceptions of Virchow and Rokitansky in the middle of the last century. The symptoms attributed to secondary infections are entirely explained either by bacillary septicemia or the destructive action of tubercle bacilli in the tissues. The occasional presence of saprophytes in the expectoration has no clinical significance. The same studies have led to a rejection of therapy by vaccines prepared from these microörganisms in the sputum.—*Recherches anatomo-cliniques et bactériologiques sur les infections secondaires dans la tuberculose pulmonaire, Piéry, Mérieux and Gliksmann, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 369.*—(*A. P.*)

Associated Infections in Pulmonary Tuberculosis.—Bezançon has rendered great service by his vigorous contributions in helping to dissipate once more the continually recurring phantom of secondary infections in pulmonary tuberculosis. The poor tubercle bacillus really has no chance. To believe certain publications, if one dies of phthisis, it is not the fault of the tubercle bacillus, but of the streptococcus, the pneumococcus, the enterococcus, or the staphylococcus. Charlatanism, masquerading as science, and advocating vaccination against secondary infections, fools not only the sick public but also the medical public, with scandalous success. It is saddening to see so many physicians using this so called therapeutic method so uncritically. In the case of tuberculosis, all useless medication is harmful, because it wastes precious time and leads to a false sense of security. Our medical periodicals are to blame for encouraging the publication of this sort of literature. It is fitting that such a congress as this meeting should condemn it and state the facts.—*Les associations microbiennes dans la tuberculose, E. Rist, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 389.*—(*A. P.*)

Associated Infections in Pulmonary Tuberculosis.—In order to make sure of the preponderance of a germ, immediate direct examination is necessary, and if a vaccine is to be prepared the culture should be made immediately. Even with these precautions, much variability of associated infections is met with. The most usual findings are: *1. Incipient cases:* Other microörganisms than tubercle bacilli are rare, the latter almost always being in pure culture. *2. Hemoptoics:* Other germs are practically confined to the post-hemoptoic period. Neither sputum examination nor blood culture has ever given proof of a superadded pneumococcic infection. *3. Acute evolutive exacerbations:* The purely caseous form rarely shows associated infections. Later in the course of disease they are often found, due to associated bronchial infection. *4. Evolutive cavities:* These are rarely infected. Infection is more apt to be found in old "cured" cavities. The indications for autovaccination seem limited to the following: 1. Old secreting cavity cases with few bacilli, apyrexia, evidence of associated bronchitis, and with a fixed type of infecting microorganism. 2. Tuberculous bronchitic cases not forming new foci, and with a fixed type of microörganism and few bacilli. 3. Exacerbations showing a single constant germ. Thus, vaccination is applicable to but few carefully selected cases; only autogenous vaccines should be used, prepared according to very precise and rigorous technique.—*Infections associées à la tuberculose pulmonaire, Essais de vaccination, M. Cordier, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 362.*—(*A. P.*)

Associated Infections in Pulmonary Tuberculosis.—Examination of the sputa of 50 tuberculosis patients showed almost regularly the presence of streptococci. Employing Kitasato's technique, Fornet and Peters, of Davos, have isolated almost always pure cultures. The vaccine prepared from them was well tolerated and its beneficial effects seemed evident. The hectic fever almost immediately became lowered and the general condition improved. Later, administration orally of an antistreptococcic vaccine, prepared by Besredka's method, proved effective.—*Le traitment spécifique des associations microbiennes de la tuberculose, W. Fornet, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 387.*—(*A. P.*)

Associated Infections in Pulmonary Tuberculosis.—These conclusions are based on a study of 144 cases and 580 careful sputum examinations. A modified method of Kitasato was used, the sputum being promptly collected and washed. In most cases tubercle bacilli alone occurred in the sputum, even in most diverse clinical types of disease. Altogether, in 81 per cent of cases they may be considered to play an exclusive rôle. *Persistently associated infections* (19 per cent): Among these are to be considered: 1. Polymicrobic infections—all terminal, the streptococcus and pneumococcus being most frequent, and associated with a bad prognosis. 2. Monomicrobic infections. Fifteen such cases were met with, 10 fatal. The tuberculosis always seemed aggravated, sometimes very suddenly

so. Among the microörganisms met with were pneumococcus, Friedländer's bacillus, streptococcus, B. coli, M. catarrhalis, M. tetragenes, B. cutis communis (staphylococcus?) and Pfeiffer's bacillus. The latter appeared to be the most benign, the two preceding most malignant. These studies furnish little basis for systematic vaccine therapy in pulmonary tuberculosis, leaving only a small group suitable for a trial of such therapy.—*Des infections associées monomicrobiennes durables dans l'evolution de la tuberculose pulmonaire, P. Courmont and M. Boissel, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 364.*—(*A. P.*)

Associated Infections in Surgical Tuberculosis.—Sorel, speaking in the capacity of a surgeon with thirty years' experience, has noted that most of the operations performed on tuberculous conditions have disastrous results and that the best treatment is usually a patiently applied hygienic-dietetic one. In ordinary microbic infections an opening of the foci is indicated, but this does not seem to play an important rôle in tuberculous foci, which are generally aggravated by such handling.—*Associations microbiennes dans les tuberculoses chirurgicales, R. Sorel, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 388.*—(*A. P.*)

Association of Tubercle Bacilli and Pneumococci in Fatal Pneumonia.—The case reported was one of caseous pneumonia in which the sputum showed both pneumococci and tubercle bacilli. At death hemorrhage into the suprarenal capsules was found. There was an old apical cavity and it seemed that the pneumonic process was primarily tuberculous. Because of the fulminating course artificial pneumothorax was not tried.—*Association de bacille de Koch et pneumocoque dans une pneumonie mortelle, P. Courmont, Boissel and Gardère, Meeting, Société Médicale des Hôpitaux de Lyon, June 3, 1924, reported in Presse Méd., June 25, 1924, no. 51, 550.*—(*A. P.*)

Associated Infections in Pulmonary Tuberculosis.—Three kinds of conditions are to be distinguished: (a) the effects of associated acute or chronic diseases in awakening or aggravating tuberculous foci; (b) the provocative action of germs entering from the exterior, and favored by the preexisting tubercle bacilli or their poisons; (c) the additional effects of the entrance of such germs into tuberculous cavities. The first point is exemplified in the case of measles, scarlet fever and smallpox. Of these, measles has the greatest effect, by reason of its lymphatic and pulmonary localizations, and its disturbance of humoral equilibrium. Syphilis also appears to render the body susceptible to tuberculosis. Concerning the second point much work has been done and it seems possible that secondary invasions play a part in certain longstanding cases, and in sudden febrile exacerbations, and contribute to the terminal cachexia.—*Infections associées secondaires à la tuberculose, P. Teissier, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 367.*—(*A. P.*)

Vegetative Nervous System in Pulmonary Tuberculosis.—Pupillary differences were seen in 50 per cent of cases with disease on one side. Facial atrophies are described in pleuritic conditions. Tachycardia depends on central or peripheral accelerating action. The common alternating constipation and diarrhea is an expression of direct toxic influencing of the intestinal ganglia and nerve ends. It is also possible that sweating is due to toxic irritation of the vegetative centre in the midbrain. The vasomotor irritability of the skin is certainly related to the outcome of cutaneous tuberculin reactions.—*Lungentuberkulose und vegetatives Nervensystem, W. Glaser, Beitr. z. Klin. d. Tuberk., June, 1923, lv, 390.*—(*H. J. C.*)

Action of Tuberculotoxins on Thyroid Gland.—The early symptoms of tuberculosis cannot be associated with functional overactivity of the thyroid. Especially contrasted are the falling out of the hair and alopecia of Basedow's disease and the rich growth of hair in tuberculosis. Histological studies showed no relation to the clinical symptoms in a way that a definite symptom-complex of pulmonary tuberculosis could be said to depend on functional disturbance of the thyroid. Only in a few cases was it possible to note an elicitation of hyperthyreosis by tuberculotoxins.—*Über die Einwirkung von Tuberkulotoxinen auf die Schilddrüse, R. Löwy, Ztschr. f. Tuberk., November, 1923, xxxix, 81.*—(*H. J. C.*)

Characteristics of Tubercle Bacilli.—An investigation into the bacteriological characteristics of 100 strains of tubercle bacilli is reported. The scope of the investigation includes the following: *1:* To isolate and cultivate tubercle bacilli from 100 consecutive cases of pulmonary tuberculosis in man. *2:* To prepare agglutinating sera against the bacilli isolated so that classification on a serological basis might be attempted. *3:* To investigate immunologi-

cal problems connected with tuberculosis. Growth was obtained directly in 100 consecutive cases of pulmonary tuberculosis, all of which had tubercle bacilli in the sputum. As digestion of the sputum is always necessary before proceeding to isolation, two methods were employed. In the first method the sputum was mixed with equal amounts of from 10 to 15 per cent antiformin and stirred until it disintegrated, which generally required only a very short time. Cultures were then made direct without centrifugating. The medium consisted of 2 parts of whole egg to 1 part of normal saline solution containing a few drops of human blood (6 drops per 50 cc.), mixed, tubed, slanted, and inspissated at 85°–75°C. for thirty minutes on two consecutive days. On this medium growth can generally be observed about the tenth to fourteenth day. When only few bacilli were present in the sputum a combination of Jousset's and Petroff's methods was adopted. In this method the sputum, if thick and tenacious, was first digested for one-half to one hour in an incubator at 37°C. with double amounts of Jousset's digestive fluid. Following this, the mixture was further digested with an equal amount of 4 per cent sodium hydrate. The homogenized solution was then neutralized with hydrochloric acid, a few drops of sterile egg-white being added to enmesh and bring down the floating tubercle bacilli, and centrifugated. The sediment was inoculated on a modified Petroff's medium containing gentian violet (1–30,000). When the sputum was not tenacious, the preliminary use of Jousset's digestive was omitted. In all cultures obtained by these methods typical bacillary forms were observed, although the majority showed the beaded type of bacillus. To obtain rapid and luxuriant growth, subculturing was done on a medium consisting of two parts of whole egg to one of 5 per cent glycerine in distilled water. Between the first and second heating of this medium 1 cc. of sterile distilled water was added to each of the tubes. Strains growing on this medium retained their viability for long periods. Subcultures made from cultures, which had been growing from ten to twelve months, in no instance failed to grow. To obtain bacilli for the production of agglutinating sera, some medium not containing egg protein was deemed necessary. As practically all strains obtained grew with difficulty in glycerine agar and broth, a special medium had to be devised. After many trials the medium described by Torrey and Buckell, plus the addition of 5 per cent glycerine and 10 gm. of *Nahrstoff Heyden* pr 1000 cc. of medium, was employed. Although not all strains of tubercle bacilli grew rapidly and abundantly on this medium, with it were achieved the best results. A satisfactory liquid medium corresponding to the Torrey-Buckell agar was finally elaborated, the only modification being that the agar used in the latter was omitted. It is extremely important that only young and vigorous cultures be employed as parent cultures, and it is also desirable that the strain should have undergone subculture on several occasions on egg before attempting to transfer it to bouillon. The article includes complete formulae for the different media used.—*The Bacteriological Characteristics of One Hundred Strains of Tubercle Bacilli Isolated from Sputum, W. J. Tulloch, W. T. Munro, G. R. Ross and W. M. Cumming, Tubercle, October, 1924, vi, 18 (to be continued).*—(*J. S. W.*)

Castration and Experimental Tuberculosis.—Four and one-half months after castration, 3 male and 3 female rabbits besides 3 control animals were infected with tubercle bacilli. The controls died earlier than the castrated animals. The castrated animals also maintiined their weight much longer after infection.—*Die Tuberkulose und die Geschlechtsdrüsen, F. M. Bricker, Ztschr. f. Tuberk., May, 1924, xl, 198.*—(*H. J. C.*)

Characteristics of Tubercle Bacilli.—In order to carry out agglutination tests it is absolutely necessary that the suspensions of tubercle bacilli be comp etely homogeneous and exhibit no signs of granularity. To ensure this it was found necessary to submit the bacilli first to the action of fat and wax solvents, and then to grind them up in saline solution. Satisfactory suspensions were obtained by extracting the bacilli with acetone and ether, using bacilli from a six to eight weeks' culture on egg medium. On theoretical grounds there is no contraindication to removing the fat and waxes in such fashion, as according to present day views these elements play no part in the antigen-antibody complex such as is employed in this serological study. This has been shown to be true with B. typhosus and B. paratyphosus, and it is considered probable that the tubercle bacillus behaves in a similar manner. The extracted tubercle bacilli are nonpathogenic for guinea pigs, being killed by exposure to the extracting agents. For the preparation of immune sera for agglutination purposes suspensions were employed, extracted as above, and inoculated intravenously into rabbits. To avoid the possibility of an egg-protein precipitin reaction occurring with the suspensions undergoing investigation, which were all grown on egg medium, tuber-

cle bacilli from agar cultures were used. By this method, several sera able to agglutinate the homologous bacillus in a titre of 1 in 200 were obtained. By appropriate tests these sera were found to be specific in their action. The 100 strains of tubercle bacilli, previously described, were serologically investigated, using three specific immune sera identical in their agglutinating powers. The results obtained were as follows: 1. There is no one member which fails to agglutinate in a dilution equal to at least one-half the titre of three type antisera, by far the greater number agglutinating to full titre. 2. There is no one member which fails to absorb the agglutinins for the type bacilli from their respective homologous antisera. 3. These three type strains are equally and mutually agglutinable by their antisera, which in turn are equally absorbable by the suspensions of both the type bacilli. *Conclusions:* 1. The tubercle bacilli recently isolated from human sputa in 100 cases of pulmonary tuberculosis all conform to one well defined serological type. 2. Certain small variations in antigenic content do exist, but these variations are negligible, being no greater than those found in other monotypical pathogenic organisms. Details of experiments and tables of results are given.—*The Bacteriological Characteristics of One Hundred Strains of Tubercle Bacilli Isolated from Sputum, Section II, W. J. Tulloch, W. T. Munro, G. R. Ross and W. M. Cumming, Tubercle, November, 1924, vi, 57 (to be continued).—(J. S. W.)*

Atypical Tubercle Bacilli.—The existence of atypical strains of tubercle bacilli has been a matter of investigation by the Royal Commission on Tuberculosis and by others. The first atypical strain was isolated by Cobbett from a case of lupus. From the work of the Commission it could be presumed, but not proved, that atypical lupus tubercle bacilli acquired their peculiar characteristics during residence in the cutaneous tissues. An alternative hypothesis was that the bacilli were already modified before they became lodged in the cutaneous tissues. Since this, investigations have been carried on by the author and others along the following lines: *1:* The determination of the presence or absence of atypical strains in other varieties of human and animal tuberculosis. *2:* The seeking of direct evidence of modification in cutaneous lesions. *3:* The determination of whether a high proportion of atypical strains is characteristic of lupus. If there were no aberrant strains, it would be possible to classify tubercle bacilli on the basis either of their cultural characteristics alone or of their virulence alone. Tubercle bacilli are, however, not always typical, and it has been found that under natural conditions they may vary from the standard, either culturally or in virulence, or in both respects. It is essential, therefore, if error in classification is to be avoided, to determine correctly both cultural characteristics and virulence. Atypical mammalian tubercle bacilli can be divided into six classes; namely, dysgonic human and eugonic bovine, attenuated dysgonic human and bovine, and attenuated eugonic human and bovine. A very careful study was made of the bacteriological characteristics of tubercle bacilli from animal and human tuberculosis. Only 7 atypical strains were found in 227 animals, including 16 fowls and other birds, infected with tuberculosis. Bovine infection largely predominated, but 31 pigs, 2 rabbits and all the birds showed avian infection. Fourteen of the remainder were infected with human tubercle bacilli. From 1100 cases of all forms of human internal tuberculosis, infected with both human and bovine bacilli, only 7 strains of attenuated bacilli were obtained. In 52 cases of scrofuloderma, a superficial tuberculous affection, attenuated strains were obtained eight times, or twenty-four times as frequently as in deepseated tuberculous lesions. Of the 15 attenuated strains obtained in all, only 6 were human and 9 bovine. The scrofulodermic atypical strains were equally divided between human and bovine, although only 38 per cent of the cases of scrofuloderma were due to bovine tuberculosis. To the pathologist lupus is of special interest because a higher proportion of atypical strains have been found in this disease than in any other variety of human tuberculosis. The author reports the results from 140 cases of lupus. Seventy-one yielded strains culturally of bovine type, and 66 strains culturally of human type, while 3 were atypical. Of the 71 bovine strains, 22, or 31 per cent, were fully virulent for all the species of animals tested, and 49 showed varying degrees of lower virulence. Of the 66 human strains, 19, or nearly 30 per cent, were of standard virulence, and 47 were less virulent in varying degree than standard human strains. Passage experiments were done with 35 of the 49 bovine atypical strains. By passage through the bodies of calves, goats or rabbits, the virulence of 13 of these strains was increased to standard. Passage experiments with human strains have not been numerous. This is because the only laboratory animal which is available for passage experiments with this type of bacillus is the guinea pig, which appears incapable of influencing the virulence of tubercle bacilli. Some observations were

made on the monkey, but this animal is unsatisfactory because it is so frequently affected with casual tuberculosis, and there is no certain method of eliminating such animals. Though passage failed to raise the virulence of 22 bovine viruses, there can be no doubt, judging from their cultural characteristics and the effects they produced on the passage-experiment animals, that these were bovine viruses which had become modified in pathogenic properties. It is also believed that the atypical human viruses were human tubercle bacilli similarly modified in pathogenic properties. A further study of these cases of lupus yielded the following interesting points: Standard human bacilli were not obtained from any patient in whom the disease had lasted longer than ten years, whereas 7 fully virulent bovine strains were derived from patients who had had lupus for more than ten years. The proportion of attenuated to standard bovine strains is not higher after twenty years than it was under five years, while in the human group the percentage rose from 50 to 100 within ten years. It is to be noted, however, that there is no clinical distinction between lupus caused by bovine tubercle bacilli and lupus caused by human tubercle bacilli. The question whether atypical lupus tubercle bacilli acquire their special characteristics during residence in the cutaneous tissues is answered in the affirmative. All the evidence goes to show that lupus is produced originally by tubercle bacilli of normal virulence, and that the virulence becomes modified during the course of the disease. Furthermore, atypical tubercle bacilli identical with those found in lupus are of very infrequent occurrence in animal tuberculosis and in human tuberculosis other than the cutaneous affections, and have not been found in the animals (cattle) or in the human beings (phthisical persons) which are the chief sources of human tuberculosis. There is no sufficient animal or human source of atypical strains, similar to those found in lupus, to account for the existence of the disease. A considerable number of cases of lupus were investigated from time to time to determine directly whether bacilli do become modified during residence in the skin. This investigation yielded the following conclusions: *1:* The lupus tubercle bacilli with modified virulence acquire their special characteristics in the lupoid lesions during the course of the disease. *2:* Cultural characteristics of bovine tubercle bacilli are very stable in the human body and constitute a more stable quality than is virulence. There is no progressive change in pathogenic properties; having acquired new characteristics, the bacilli then remain stable for an indefinite period. What is the explanation of this frequent modification of the pathogenic properties of tubercle bacilli in lupus? It has been suggested that the action of daylight, subnormal temperature, local treatment, etc., might bring about the change. There is, however, no demonstrable relation between attenuation and the degree of exposure to light. Fully virulent human and bovine strains have been obtained from lesions on the face and neck which had been in existence for years. On the other hand, human and bovine strains with modified virulence were obtained in cases in which the lesions were on the trunks and legs. Lupus is very commonly situated on the face, neck and extremities, parts of the body which were relatively cool, and this suggested the hypothesis that subnormal temperature might have an influence on the virulence of the bacilli. To test this hypothesis, passage experiments were done with toads using a bovine strain of tubercle bacilli. Prolonged residence (seven years) in such cold-blooded hosts did not cause any decrease or alteration in cultural characteristics. Treatment of the lesions with antiseptics, Finsen light, etc., was certainly not the cause of the modification, as the majority of cases under consideration had not been treated in any way. If they had been the cause, the modification would be progressive and the disease would gradually diminish in severity. But observations have all failed to show a progressive alteration in pathogenicity; having become more modified, the bacilli retain their new characteristics for an indefinite period. Moreover, lupus produced by modified tubercle bacilli is not a milder process than lupus caused by fully virulent bacilli. On the contrary, the disease in these cases is characterized by persistence, intractability, and tendency to spread. Although the tubercle bacilli have lost virulence for experimental animals there is no loss, rather is there an increase, in the virulence of the bacilli for the individual affected with lupus. It is concluded that the changes in virulence of tubercle bacilli observed to occur during residence in lupus lesions are not merely degenerative, but are the result of adaptation of the bacilli to conditions in the skin. The nature of these conditions, which do not apparently obtain in the organs, is obscure.—*Atypical Tubercle Bacilli in Human and Animal Tuberculosis with Special Reference to Those Occurring in Lupus, A. S. Griffith, Tubercle, September, 1924, v, 569.*—*(J. S. W.)*

Transmutation of Tubercle Bacilli. In 1911 Eber reported the transmutation of human to bovine tubercle bacilli by coinci-

dent intraperitoneal and subcutaneous injections into cattle. The tissues were supposed to contain substances which favored this change. Neufeld with Dold and Lindemann obtained only negative results in similar experiments. In later experiments Eber and Lange believed that they noted an approach of the human bacilli to the bovine type. The work of Eber is analyzed in detail and criticized, and it is shown that such findings as were interpreted to be transmutation were not properly evaluated, and were findings easily within the normal habits of the bacilli, even before they had been inoculated into cattle or rabbits. Changes in virulence of the bacilli and the significance of bovine tuberculosis for man are discussed in detail. Neufeld does not agree with Eber in the ready transmutation of human to bovine bacilli.—*Zur Frage der Tuberkelbacillentypen, F. Neufeld, Beitr. z. Klin. d. Tuberk., June, 1923, lvi, 48.*—(*H. J. C.*)

Cultivation of Tubercle Bacilli from Spinal Fluid.—In the meningitis division of the New York City Department of Health it has been the custom to use guinea pigs for isolating tubercle bacilli from the spinal fluid of cases of tuberculous meningitis. The animals are later killed and cultures for typing made on suitable media. Owing to the fact that guinea pigs often die of accidental infections before definite lesions can be demonstrated an attempt was made to cultivate the bacilli by direct planting upon artificial media. The technique was as follows: As much spinal fluid as possible (including web, if present) was centrifugated at high speed in the ordinary conical centrifuge tube for two hours. All but 0.5 to 1 cc. of the supernatant fluid was poured off and discarded. After being resuspended by agitation and scraping, the sediment was removed from the tube with a sterile pipette and distributed over the surfaces of five slants,—two Dorset egg, two Lubenau's and one coagulated blood agar. The last served as a control for contaminating organisms. Petroff's medium was not found necessary, as spinal fluids are seldom contaminated. All plantings, from which tubercle bacilli grew, showed good growth in from twenty-one to twenty-eight days. Of the 34 sediments planted, 25, or 73.3 per cent, yielded positive cultures; 6 remained sterile, perhaps because of paucity of material, and 3 showed contaminations on both the egg media and the control shortly after planting. Of the 25 which yielded growth of tubercle bacilli, 2 were from sediments which after prolonged search failed to show acid-fast bacilli on smear, and 2 showed acid-fast granules (granules of Much). Whenever the amount of spinal fluid permitted, direct guinea-pig inoculations were also done. This was carried out with fluids using 2 guinea pigs for each. Four sets died within a week to ten days after inoculation and showed no lesions. Yet the cultures of the sediments from these same spinal fluids yielded tubercle bacilli. The results obtained by the direct cultural method were compared with those previously obtained by animal inoculation. A series of 34 consecutive fluids were taken, some showing positive smears, and some apparently negative, and it was found that the percentage of positive results was the same for both methods. From the above it is evident that if the amount of fluid permits, the direct cultural method, in addition to the animal inoculation, may be the means of confirming the diagnosis and also the saving for further study of a strain which otherwise might be lost if animal inoculation alone is relied upon. Of course, if the spinal fluid is contaminated inoculation into the guinea pig will often result in lymph nodes from which the tubercle bacillus may be grown in pure culture. A series of 48 strains of tubercle bacilli isolated from spinal fluids from cases of tuberculous meningitis showed 3, or 3.3 per cent, to be of bovine origin. Typing was done by cultures. In case of doubt as to type, rabbit inoculation was also done.—*Direct Cultivation of Tubercle Bacilli from Spinal Fluids, Occurrence of Human and Bovine Types, R. Gosling and J. Montanus, J. Med. Research, September, 1924, xliv, 513.*—(*J. S. W.*)

Growth-Inhibiting Effect of Chaulmoogra Oil on Acid-Fast Bacilli.—In a search for an understanding of the direct action of chaulmoogra oil on acid-fast bacteria, an effort to change the atomic arrangement of these agents or add new groups to them has been made. The resin of palomaria oil is the probable inhibiting element in this substance. The essential oils inhibit growth of acid-fast bacilli by their volatile elements, but this is not true of chaulmoogra oil. Two properties of chaulmoogra oil are probably involved in producing a growth inhibition; "namely, the degree of unsaturation and the chemical structure of the fatty acids, the latter differing radically from the structure of the fatty acids obtained from any other known vegetable oil." But more than merely the degree of unsaturaton is shown by experiment to be involved. The unsaturation of oils containing acids from the chaulmoogra series and of certain growth-stimulating oils is paramount. Saturated chaulmoogra oil does not inhibit growth of acid-fast bacteria; unsaturated chaulmoogra

does. The growth-inhibiting element in this product depends on the structure of the fatty-acid ring. Hydrogen saturation changes the ring and does away with its capacity to inhibit growth. Acid-fast bacteria adapt themselves to chaulmoogra oil in time and develop a tolerance to it.—*Chemotherapeutic Experiments with Chaulmoogra and Allied Preparations. V. An Inquiry into the Mechanism and Nature of the Growth-Inhibiting Effect of Chaulmoogra and Other Vegetable Oils, O. Schöbl, Philippine J. Sci., August, 1924, xxv, 135.—(H. S. W.)*

Growth-Inhibiting Effect of Organic Compounds on Acid-Fast Bacilli.—Water-soluble compounds have an antiseptic effect on tubercle bacilli *in vitro* but fat solvents have but little such effect. Sodium, copper and nickel salts are effective. The double-bond-containing compounds and unsaturated alcohols are also antiseptic, as are hydroxy compounds and phenols. Tables show the relative antiseptic effect of a large number of compounds.—*Chemotherapeutic Experiments with Chaulmoogra and Allied Preparations. IV. A Survey of Certain Organic Compounds as to Their Growth-Inhibiting Activity toward Acid-Fast Bacilli in Vitro, O. Schöbl, Philippine J. Sci., August, 1924, xxv, 123.—(H. S. W.)*

Effect of Alcohol on Inspired Bacteria.—There is a general belief that alcohol exerts a harmful influence on the natural defenses of the body. The fact that alcoholic intoxication increases the susceptibility of animals to a number of infections is recognized. A study was done to compare, in normal and intoxicated mice, the time of disappearance from the lungs of inspired pneumococci, hemolytic streptococci and influenza bacilli, and the relative occurrence of generalized infection in the gwo groups of animals following the inhalation of pneumococci. The test animals were allowed to inhale an atmosphere in which a fine bacterial mist had been produced by spraying a culture of the germ to be studied. The mice were intoxicated by intraperitoneal injections of 1.5 cc. of 10 per cent alcohol in normal salt solution. The following conclusions were arrived at: 1. When mice are exposed to an atmosphere containing certain bacteria in the form of a fine mist, the bacteria may be recovered from the deeper respiratory passages. 2. Pneumococci which have reached the lungs of normal mice as a result of this procedure usually disappear within a few hours and give rise to no generalized infection. In mice intoxicated with alcohol, on the other hand, pneumococci persist in the lungs for a longer period and fatal septicemia frequently follows. 3. Hemolytic streptococci and B. influenzae generally persist in the lungs for about twenty-four hours. In intoxicated mice these germs do not disappear so rapidly from the lungs, and generalized infection is much more frequent. 4. These experiments yield no evidence as to how alcoholic intoxication renders the lungs more permeable to inspired bacteria. But they do show that alcohol delays the removal of inspired bacteria from the lungs and favors the invasion of the blood stream.—*Persistence of Inspired Bacteria in the Lungs of Alcoholized Mice, E. G. Stillman, J. Exper. M., September 1, 1924, xl, 353.—(J. S. W.)*

Chemical Analysis of Tubercle Bacilli.—These studies were mostly carried out from 1910 to 1914. A nucleoprotein extract of the tubercle bacillus was prepared by drying living cultures in a vacuum and then extracting them with petroleum ether and sulphuric ether; the bacillary bodies were then boiled in a sodium-carbonate solution, allowed to settle, and precipitated by an acetic-acid solution, the process being repeated several times. Fine cultures were obtained with suitable mineral solutions, adding a mono or diamino-acid, such as glycerine. The best media contained argynine or glycocol.—*Analyse chimique du bacilli tuberculeux, P. Armand-Delille, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 399.—(A. P.)*

Chemical Analysis of Tubercle Bacilli.—Bezançon describes the variability of the morphology of bacillary colonies according to the medium. On a potato medium they are scarcely recognizable as more than acid-fast bacilli. On a liquid medium the growth is largely colorable by methylene blue, and acid-resistant forms are rare. Thus, acid-fastness seems to vary with the richness of the medium. Age also causes variations in morphology. The bacilli from old cultures are granular and full of gentianophile bodies.—*L'analyse chimique du bacilles tuberculeux et les milieux de culture, F. Bezançon, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 397.—(A. P.)*

Rôle of Lipoids of Tubercle Bacillus.—Whatever the exact chemical composition of these lipoids, we cannot ignore their relationship with the bacillary proteins. Lecithins and proteins can, according to Mayer and Terroine, form compounds having the characteristics of solubility of the lecithins. The study of the bacillary phosphatids is most important, because the

lipoids, either by themselves or combined with proteins, play an important part in the general phenomena of tuberculosis. *Antigenic properties:* Much considers only the neutral fats active; Kurt Meyer gives the phosphatids the antigenic function, a view borne out by experiments carried on since 1920. *In vivo* the phosphatids provoke in new animals abundant antibody formation; *in vitro*, in the presence of tuberculous serum, they fix complement more strongly than the whole bacilli, and are quite specific. The residue after partial acetone extractions, soluble in methyl alcohol, deviates complement in the presence of tuberculous serum. Complete acetone extraction, however, diminishes their antigenic power. Methyl alcohol also extracts a substance which behaves *in vivo* like tuberculin, and is regarded as a polypeptid; but it produces no antibodies and does not deviate complement. The lipoids separated from this tuberculin, however, preserve an antigenic value equal to the original mixture or solution. The acetone-insoluble substances which have no antigenic power *in vitro* produce some characteristic reactions on injection into animals. Finally, the residue after both acetone and alcohol extraction loses all antigenic power, but retains the reactivating properties of proteins, being able to produce Koch's phenomenon in guinea pigs. The importance of the lipoid constituents of tubercle bacilli is emphasized, especially that of the phosphatids.—*Sur le rôle des lipoides du bacille de Koch, A. Boquet and L. Nègre, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 390.*—(*A. P.*)

Lipoidal Bacteriolysis of Tubercle Bacilli. Prolonged action of lipoidal substances on tubercle bacilli leads to all stages of lipolysis, from simple loss of acid-fastness to complete solution of the microörganism. Of the lipoidal substances used, lecithin, olive oil and green soap were most effective. When the destruction was most marked many Much forms were left. Lanolin produced many "fuchsin-bodies," but numerous acid-fast forms also persisted. Tubercle bacilli treated 4 to 6 weeks with oleic acid and olive oil lost their virulence completely. Cholesterol in alcoholic solution led to little change in the morphology or staining capacity of tubercle bacilli. A few granular forms were produced, but a majority of the bacilli retained the normal staining power. Glycerol was without effect on the bacilli. After cholesterol and glycerol treatment the bacilli still grew on culture media. Under the action of green soap bacillary forms gradually disappeared while granular forms increased, and after 6 weeks' inoculation of culture media led to no growth. No appreciable result followed the action of potassium and sodium salts. On treatment with alkalies acid-fastness disappeared, leaving blue rods, but on sufficient washing out of the alkali acid-fastness returned to some extent. Alcoholic solution of lecithin in 1:25 concentration led to the production of granular forms in 7 to 9 days. After 6 weeks' action of water solution of lecithin only a few non-acid-fast forms and numerous granular forms persisted, and inoculation of culture media led to no growth. Such marked bacteriolysis suggests new lines of study of the immunity and therapy of tuberculosis.—*Zur Frage über die Bakteriolyse der Tuberkelbazillen, M. Isabolinsky and W. Gitowitsch, Ztschr. f. Immunitätsforsch. u. exper. Therap., July 30, 1924, xl, 303.*—(*E. R. L.*)

Defatting Tubercle Bacilli.—In studying the chemical constitution of tubercle bacilli it is sometimes desirable to eliminate the fatty substances without altering the albuminous constituents. This is done by applying fat solvents in the form of vapors. Treatment by ether vapor requires only ten minutes, as compared to several hours with liquid ether. The bacillary emulsion then settles out in three layers: (1) the lower layer, composed of unaltered bacilli, (2) the intermediate layer, consisting of defatted bacilli, non-acid-fast and (3) the upper layer, resembling cream, and consisting almost entirely of fats. On treatment successively by different solvent vapors, one obtains different fractions of fatty matter. The intermediate layer represents quite a stable emulsion of more or less defatted bacilli, which lend themselves well to agglutination experiments and may be employed in diagnostic reactions.—*Le dégraissage de bacilles tuberculeux, W. Fornet, V^e Congrès National d. l. Tuberc., reported in Rev. d. l. Tuberc., 1923, no. 4, 398.*—(*A. P.*)

Immunity to Tuberculosis.—Tuberculosis immunity exists only as a result of an infection with tubercle bacilli of sufficient virulence. It requires a latent infection to produce immune bodies. Tuberculin is a specific irritant which, without being bound by the susceptible cell, produces a specific inflammatory reaction. The investigation of the changes in the cell produced by a tuberculous infection remains a problem of greatest interest. A mild allergy, which occasions a suitable immunity in man, is the most efficient. Therapeutically, the subcutaneous administration of tuberculin is preferred, since it is not believed that the skin is an important organ in immunity. For diagnostic purposes the local reactions

are the most suitable; the Pirquet cutaneous reaction, as the simplest but least exact, must under certain circumstances be elaborated upon by one or two intracutaneous or subcutaneous puncture reactions. The tuberculization of the populace is general and in combating human tuberculosis must be considered. Infection during childhood must not occur too early or be too massive. If a child develops disease suitable treatment should be instituted, preferably in a sanatorium. In adults the resistance is to be increased by improving nutrition to prevent development of the disease.—*Die Tuberkuloseim-munität auf Grund der heutigen Kenntnisse, H. Selter, Beitr. z. Klin. d. Tuberk., June, 1923, lv, 318.*—(*H. J. C.*)

Passive Sensitization to Tuberculin.—Bail's experiments, for which a passive transference of tuberculin sensitiveness was claimed, as the result of injection of organ emulsions of tuberculous animals into normal animals, were repeated. Klopstock injected organ emulsions of tuberculous animals and defibrinated blood, together with tuberculin, into normal guinea pigs. In the majority of instances the animals showed no immediate evidence of injury or poisoning. In a few cases the guinea pigs died within 36 hours, but control experiments in which organ emulsions, but no tuberculin, were injected, showed that this effect might well be due to the emulsion alone. Thus no support was lent by these experiments to the theory that the general tuberculin reaction and the skin reaction are to be attributed to the formation of a toxic substance on the interaction of tuberculin and sensitized tissue.—*Zur Uebertragung der Tuberkulinempfindlichkeit, F. Klopstock, Ztschr. f. Immunitätsforsch. u. exper. Therap., June 25, 1924, xl, 27.*—(*E. R. L.*)

Anaphylaxis and Tuberculin Reaction.—The tuberculin reaction should be regarded as a phenomenon of allergy or hypersensitiveness and not as a manifestation of anaphylaxis for (among others) the following reasons: (1) Anaphylactic reaction is immediate; tuberculin reaction occurs only several hours after injection. (2) In anaphylaxis there is a drop in temperature; in the tuberculin reaction there is an elevation of temperature. (3) The anaphylactic state can be passively transferred to normal animals by tranfusion of blood from the sensitive animal to the normal; transfer of serum from tuberculous to normal animals carries no transfer of tuberculin-reaction capacity. (4) Anaphylactogens have no deleterious effect locally on tissues; tuberculin causes local necrosis of tissue in the tuberculous animal. (5) Anaphylactogens are proteins and sensitize normal animals; tuberculin has not been proved to be protein and does not sensitize.—*Anaphylaxis and the Tuberculin Reaction, A. B. Crawford, J. Am. Vet. Med. Assn., October, 1924, lxvi (new series, xix), 18.*—(*H. S. W.*)

Allergic Irritability.—As a matter of physiology the production of immunity or hypersensitiveness would appear to involve the conception of stimulation, and the capacity to be stimulated involves the conception of irritability. Thus the term *allergic irritability* is proposed as a general characteristic of the animal, on the basis of which it reacts to stimuli of the antigenic class, whether they be helpful, injurious, or indifferent to bodily health. Antibodies against the tubercle bacillus are formed in relatively small amounts, and with difficulty, by any species. In the case of the guinea pig, they have been scarcely more than occasionally demonstrated. While studying the mechanism of the production of antibodies, in general, in the guinea pig, the authors were led by an accidental occurrence to carry through an experiment designed to show whether a preexisting tuberculosis affected the production of antibody for an antigen unrelated to the tubercle bacillus. The result was definite, showing a decided increase in antisheep amboceptor production by tuberculous guinea pigs. Twenty guinea pigs were inoculated intraperitoneally with 0.01 mgm. of bovine tubercle bacilli. An equal number of animals were put aside as controls. At the end of three weeks all were inoculated with 10 cc. of a 20 per cent suspension of washed red blood-corpuscles of the sheep. One-half of this was given intraperitoneally and one-half subcutaneously. On the thirty-third day succeeding, the surviving animals were again injected with the same amount of sheep corpuscles. The animals were bled from the heart on the third day following the first injection of corpuscles, and at frequent intervals until the forty-first day. In comparing the amboceptor production of the two groups, it was found that preëxisting tuberculosis greatly increased the amount of amboceptor formed. At the point of maximum production, and on the average, this difference may be as much as twenty fold. No animal in the control series produced as much antibody as the least active of the series with tuberculosis. The form of the curve of antibody production is the same in both groups. This would seem to suggest that the effect of the tuberculosis is one of stimulation to a normal mechanism, or possibly that the cellular basis of such a mechanism is hypertrophied, rather than that any wholly new

factor has been introduced by the disease. The condition underlying increased amboceptor production in the first series was fully established when the blood corpuscles were injected, judging by the immediate increased response in the tuberculous guinea pigs. A second series of pigs were treated similarly to the first except that infection with tubercle bacilli was only two days before the injection of the blood cells. This experiment was designed to develop the point in the tuberculous infection at which the influence in question becomes manifest. With the dosage and culture used it was found that the effect on amboceptor production was invariably present and sustained after the seventeeth day. Thus, these experiments show that in tuberculous guinea pigs there is a very marked increase in the amount of antibody produced in response to a given injection of antigen from the time the disease is well established. Although the body may be very much occupied with one microörganism (that is, one antigenic complex) it has not lost its capacity to react to an unrelated one. It is evident that in tuberculosis that character which is designated as allergic irritability is high with respect to an antigen not related by origin to the tubercle bacillus. These experiments indicate that when we are dealing with the "capacities" which must underlie the phenomena of immunity, whether natural or acquired, the rules of specificity are no longer a sure guide to either experiment or interpretation.—*Allergic Irritability. The Formation of Anti-Sheep Hemolytic Amboceptor in the Normal and Tuberculous Guinea Pig, P. A. Lewis and D. Loomis, J. Exper. M., October 1, 1924, xl, 503.*—(*J. S. W.*)

Skin Hypersensitiveness with Dead Tubercle Bacilli.—In a recent publication the author has shown that true tuberculin skin hypersensitiveness can be set up in normal guinea pigs after injections of tubercle bacilli killed with heat, and that such hypersensitiveness is indistinguishable in all its fundamental and essential respects from that observed in animals inoculated with living tubercle bacilli. Observations are now reported concerning the duration of the hypersensitiveness. Two guinea pigs, each receiving, in divided doses, 37.5 mgm. of dead tubercle bacilli killed by heating for one hour at 100°C., definitely reacted to tuberculin intracutaneously three hundred and fifty-eight days and four hundred and ninety-seven days from the beginning of the experiment, respectively. In another series animals received, in all, 3.75 mgm., 7.5 mgm. and 18.75 mgm. of dead tubercle bacilli for purposes of sensitization. All gave positive skin tests, usually within eleven days, and the skin hypersensitiveness persisted for various periods of time. It is to be noted that even as small an amount of killed tubercle bacilli as 3.75 mgm. can set up a skin hypersensitive state, which persisted in one animal for three hundred and eighty-two days. There was no question as to the sterility of this material because in no instance was there generalized tuberculosis. When tubercles were present in the peritoneum they were the result of dead bacilli. It is very likely that skin hypersensitiveness persisted in all these animals for the reason that foreign particles of tubercles were present in the animals. The success of this sensitization depends on the following few points: The tubercle bacilli must be triturated well, made up in good suspension, and the reaction adjusted to pH 6.9 or 7.0 before sterilization. Above all, one of the most important points is that animals suitable for such sensitization must weigh 400 gm. or over. The injection should be made every three or four days, and the intraperitoneal route is the most suitable one.—*Immunological Studies in Tuberculosis, II. Further Observations on Skin Hypersensitiveness in Experimental Tuberculosis, S. A. Petroff, J. Immunol., July, 1924, ix, 309.*—(*J. S. W.*)

Allergy Due to Dead Tubercle Bacilli.—The animals were all tested prior to injection of dead tubercle bacilli and thus proved healthy. Intracutaneous tests after preparatory treatment with heat-killed bacilli proved positive. Heating in a steam boiler two to three times for 45 minutes resulted in weaker intracutaneous tuberculin reactions than if the bacilli had been heated only once for 45 minutes in a steam boiler.—*Über die Hervorrufung von lokaler Tuberkulinempfindlichkeit bei gesunden Meerschweinchen vermittels subcutaner Vorbehandlung mit abgetöteten Tuberkelbacillen, E. Boecker and J. Nakayama, Ztschr. f. Hyg., 1923, ci, 11.*—(*H. J. C.*)

Allergy Due to Dead Tubercle Bacilli.—Local tuberculin hypersensitiveness in guinea pigs was produced by means of two to three subcutaneous, or subcutaneous and intraperitoneal injections of heat-killed human tubercle bacilli. Only one animal proved refractory. The intracutaneous tests were made seventeen to thirty-three days after the last preparatory treatment. The results did not differ from those obtained with mild or moderate tuberculous infection. By utilizing this information it is hoped that the problem of the relation of the allergic condition to the relative protection against

a second infection is being more nearly approached.—*Über die Hervorrufung von lokaler Tuberkulinüberempfindlichkeit bei nichttuberkulösen Meerschweinchen vermittels parenteraler Vorbehandlung mit abgetöteten Tuberkelbacillen, E. Boecker, Ztschr. f. Hyg., 1923, ci, 1.*—(*H. J. C.*)

Infection and Reinfection by Dead Bacilli in Rabbits.—Since the work of Prudden and Hodenpyl it has been known that injection into the veins of the rabbit of an emulsion of killed tubercle bacilli may produce pulmonary tubercles within 15 days, which, however, according to these authors, never caseate. Straus, however, claims to have observed caseation, and also states that if the emulsion be very fine no macroscopic lesions result. Coulaud has repeated these experiments and finds that to produce death over 0.05 gm. are necessary. Doses under 0.01 gm. ordinarily result in two or three granulations on the posterior border of the lung, sometimes a single tubercle, which usually scleroses rapidly, the reverse of the case when living bacilli are used. Coulaud then tried emulsifying bacilli in oil after killing them by heat (one hour in the autoclave at 120°C.). Each rabbit received 0.02 gm. Animals killed between the tenth and twentieth days showed extensive pneumonic lesions throughout both lungs. From the twentieth to the fortieth day nodules appeared and later there was observed limitation and evolution towards cure. Reinoculations were practised on 10 animals, and similar lesions were obtained. Necrosis and caseation of the pneumonic areas occurred if the dose was large. Six other rabbits were inoculated with killed and partially defatted bacilli, and in these cavity formation was observed. Intravenous injection of dead bacilli does not affect the spleen or kidneys, but the liver shows leucocytic and lymphocytic infiltrations. Horse glanders bacilli, on the other hand, killed and emulsified either in oil or physiological saline solution and injected intravenously, caused no lesions of consequence in any organ. It is known that the reinoculation of dead bacilli often causes fatal accidents. Rabbits which have received doses of 0.001 gm. of dead bacilli intravenously react to tuberculin and this reaction lasts about three months, disappearing in about the same time as the lesion produced by injection. It is not possible, however, to kill such rabbits by tuberculin, even using as much as 0.5 cc. intravenously. —*Infection et reinfection par les bacilles morts chez le lapin, E. Coulaud, section d'etudes scientifiques d l'Oeuvre, d. l. Tuberc., April 12, 1924, reported in Rev. d. l. Tuberc., June, 1924, v. 415.*—(*A. P.*)

Tuberculin Skin Reaction after Operation.—Tests were made on 86 subjects during the first week after operation. Of 20 operated on under chloroform 25 per cent were negative; of 40 under ether, 40 per cent; and of 26 under regional anesthesia, 7 per cent. It is believed this indicates the relative differences in toxicity due to type of anesthesia.—*Contribution à l'étude de la cuti-réaction à la tuberculine chez les opérés, G. Decressac and A. Jacquelin, Meeting, Société de Biologie, June 28, 1924, reported in Presse Méd., July 2, 1924, no. 53, 560.*—(*A. P.*)

Inactivation of Serum Lipase with Tuberculin.—In an earlier study it was shown that serum lipase is inactivated *in vitro* by tuberculin. By this method a number of different tuberculin preparations were tested. The tuberculins were O. T., Cutituberkulin Höchst, O. T. and diagnostic tuberculin Merck, and tuberculin Rosenbach. The most marked inactivation of lipase occurred with diagnostic tuberculin and O. T. Merck, as well as with O. T. Höchst. Following in order after this were Cutituberkulin Höchst and tuberculin Rosenbach. The most marked inactivating action upon serum lipase occurred with preparations most valuable for the cutaneous reaction. Exceptional, however, in this respect appeared tuberculin Rosenbach, which proved valueless for the cutaneous reaction but was powerfully inactivating for serum lipase. It was shown that serum lipase is inactivated by nutrient broth as well as peptone alone, so that it is believed that the action to the tuberculin lipase can be attributed to its peptone content.—*Die Prüfung von Tuberkulinpräparaten in vitro mit Hilfe der Serumlipasevergiftung, C. Falkenheim and P. György, Beitr. z. Klin. d. Tuberk., June, 1923, lv, 466.*—(*H. J. C.*)

Dust Inhalation in Guinea Pigs.—The experiments reported in this article on the lesions produced in guinea pigs by the inhalation of certain dusts were undertaken on behalf of the Medical Research Council (Great Britain). Over 100 animals were used in the course of observations extending over a period of two years. The origin of the dust cells and the modes of elimination of the dust particles from the lungs were carefully studied; also the relationship between the degree of harmfulness of a given dust and the degree of sharpness and angularity of its constituent particles. In exposing the animals to dust the Mavrogordato apparatus was used. This consists of a large wooden box with a two-bladed fan working in a circular channel at its bottom.

The animals were placed on a wire grid midway between the top and bottom of the box. The animals were "dusted" for two hours daily over a period of twelve days. The dusts were measured by volume, and the total amount of dust placed in the machine for each period of two hours was 135 cc. Animals were killed by severing the carotid under chloroform anesthesia. To reduce collapse of the lungs to a minimum, the trachea was ligated before opening the thorax and removing the lungs. For purposes of microscopic study the lungs were imbedded in paraffin under reduced atmospheric pressure. The following dusts were used: (1) flint and coal mixture, (2) china clay, (3) ground pitcher (crushed up earthenware after firing), (4) feldspar, (5) pure amorphous silica, (6) pure flint, (7) coal, (8) slate, (9) ignited shale (all organic matter destroyed), (10) dried earth and (11) ignited earth. In a bacteriological examination of sections from "dusted" animals neither tubercle bacilli nor any lesions even remotely suggesting pulmonary tuberculosis were ever noted. In considering the results obtained it is important to recognize that the pulmonary response of the guinea pig is often different in degree from that of man. Thus, fibrosis, the outstanding lesion directly due to the inhalation of flint dust in man, was never produced by an intake of pure flint into the lungs of guinea pigs in these experiments. Again, the nasal filter of the guinea pig appears to be greatly superior to that of man; hence, the actual dust-content in inspired air would be less in the guinea pig than in man. Finally, when working with animals, it is necessary to restrict the time of exposure to as short a period as possible, whereas a man employed in a dusty trade inhales dust for many years. Hence the necessity of using very high concentrations of dust in the case of animal experiments, in order to obtain definite lesions after so short a series. The lesions produced by the different dusts employed in these experiments are described and discussed separately in great detail. China-clay dust apparently was most harmful of all the dusts employed. Yet there is no evidence that this dust is particularly harmful to the lungs of human beings. Feldspar, which is also used in the manufacture of china and earthenware, also proved to be a harmful dust. Pure silica only occasionally caused fibrosis in the animals, and the inhalation of flint never; yet the inhalation of flint dust is notoriously deadly, as testified by the mortality in certain trades, especially flint-knapping, from pulmonary disease. The evidence derived from these experiments is against the view that the degree of harmfulness of a dust is proportionate to the degree of angularity and sharpness of its constituent particles. Nor has the supposition, that the dusts which stimulated phagocytosis were those which contained organic matter, been confirmed experimentally. Although silica may be regarded as a cell poison and this may account for the inability of the phagocytes to remove it, there are probably other factors than this, since shale—universally admitted to be one of the least harmful dusts—contains from 55 to 60 per cent of silica. As to why one dust is harmful and another not, is a problem as yet unsolved. The presence of *plaque-formation* was interpreted as indicating permanent damage to the lungs caused by the dust. Plaques are conglomerations of thin squamous-like cells, the cytoplasm of which is packed with dust particles. The nuclei of such cells are often multiple, and degenerate. There is evidence to show that the large plaques which tend to be formed in the parenchyma represent permanent pulmonary lesions. Small plaques, on the other hand, may be formed within the pulmonary lymphatics, in which case they may disintegrate in course of time. Such plaques have been termed *intralymphatic plaques*. In discussing the origin of the dust cell the belief is justified that dust cells are frequently derived from the alveolar epithelium. This, however, does not exclude the possibility of some participation of leucocytes or endothelial cells in the phagocytosis of dust particles. With regard to the modes of elimination of dust from the lungs it is shown that the dusts which stimulate phagocytosis tend to be eliminated from the lung by both bronchi and lymphatics, while such elimination as occurs of the dusts which elicit but a feeble phagocytic response is through the lymphatics rather than the bronchi. This very complete article includes many reproductions of microphotographs of sections from the lungs of normal and dusted animals.—*The Pulmonary Lesions Produced by the Inhalation of Dust in Guinea Pigs. A Report to the Medical Research Council, H. M. Carleton, J. Hygiene, July, 1924, xxii, 438.*—(*J. S. W.*)

Topography of Traube's Semilunar Space.—Numerous descriptions of Traube's semilunar space have been made. They all agree in general but differ in details of the upper boundary of the space. This study was made on 50 subjects examined radioscopically, and on 9 cadavers the organs of which were fixed *in situ*. The following conclusions were arrived at: *A:* The space is bounded below by the left costal margin from the anterior extremity of the eighth costal cartilage to the anterior axillary line;

generally this line crosses the costal margin at the level of, or in the neighborhood of the anterior extremity of the eleventh rib. Above, it is limited by a curved line concave downward and inward. This line corresponds to the anterior border of the liver extending from the anterior extremity of the eighth costal cartilage to the sixth sternochondral articulation. The line then follows the inferior border of the left lung to the point where the eighth intercostal space is crossed by the anterior axillary line. The superior boundary of Traube's space then changes its direction a third time and descends vertically along the axillary line, in front of the spleen, to the free extremity of the eleventh rib. Contrary to the classical opinion, the heart and pericardium are a little above Traube's space. *B:* The tympany on percussion of the space may be due to stomach, gastrocolonic, or colonic tympany. This depends on the physiological state of the digestive tract. *C:* The relations of the stomach and colon to the abdominothoracic parietes are almost invariable in three regions, irrespective of their fulness or the position of the subject, which are the fixed points or points of attachment of these organs. These three regions are (1) the cardiac orifice region, (2) the region of the pylorus and duodenum and (3) the splenic angle. *D:* With the exception of these fixed points all other parts of the stomach and colon are movable and their positions variable. The stomach, fixed along the line of the cardiac orifice and pyloric canal, is gathered against the vertebral column when it is empty, and pulls the colon toward it by the gastrocolic ligament. The former, with its fixed splenic angle, can thus occupy the left half, or even more, of the semilunar space. The distended stomach occupies as much as three-quarters and even more of this space, proportionately reducing the colon space. The respiratory movements and the displacements which the vertebral column imposes, chiefly in the duodenal region, in the transformations which it brings about according to the position of the subject,—dorsal decubitus, right lateral or left lateral,—do not modify in any important manner the topography of the left subdiaphragmatic space, and consequently that of the semilunar space of Traube. *E:* The following are the pathological states of the organs contained in Traube's space and of the neighboring organs which bring about the greatest changes in the left subdiaphragmatic space: gastric atony, visceroptosis, hypertrophy of the liver and the spleen, cysts of the pancreas, hypertrophy of the heart, large pleural and pericardial effusions, and the different tumors, benign and malignant, of the regions cited.—*Contribution à l'étude topographique de la loge sous-phrénique gauche et de l'espace semilunaire de Traube, D. Berceanu, Presse Méd., July 23, 1924, no. 59, 622.*—(*B. T. McM.*)

Quality of Breath-Sounds.—By analyzing the qualities of loudness, timbre, tone and purity it was possible to determine causally, and define individually, the physiological and pathological breath-sounds, and thus avoid lack of clarity in definition and classification. Loudness with intensity makes the breath-sounds appreciable. Absolute or relatively loud and soft breath-sounds can be differentiated. Timbre is exhibited by the greater number of pathological breath-sounds. Among the clinical associated sounds more groups are differentiated empirically. As the physiological basic breath-sound we note quiet vesicular breathing. In pathological conditions there can be differentiated the vesiculobronchial, the bronchovesicular, and bronchial or amphoric breathing. The like or unlike qualities of the breath-sounds indicate their origin. The tone is insignificant practically, but theoretically it is of interest.—*Über die Qualitäten der Atemgeräusche, A. Winkler, Beitr. z. Klin. d. Tuberk., June, 1923, lv, 308.*—(*H. J. C.*)

Adventitious Sounds in Healed Lung Tuberculosis.—Healing in tuberculosis must be diagnosed with great caution and, in the abstract, the only justification of the term would be in cases in which there would be absolute demonstration that all bacilli have been eliminated from the body. This is impossible, and it is much better to use such terms as "latent," "inactive," etc. With this in view, treatment of the disease becomes much different, for now the doctor must see to it that the patient is sheltered in his work and that all possible means are used to safeguard the patient's health. As to the adventitious sounds in old tuberculous lungs, it is impossible for the skilled physician to tell whether old scars or a nearby fresh, exudative process is producing the sounds.—*Narbengeräusche bei geheilter Lungentuberkulose, Stroux, Deutsche med. Wchnschr., May 16, 1924, i, 644.*—(*H. S. W.*)

Auscultatory Percussion.—The various modifications of auscultatory percussion and palpation, when properly employed, give data regarding the size of both solid and air-containing viscera not equalled in clinical value by any other known diagnostic method; and only approximated by roentgen ray findings. In a study of the lungs, auscultatory percussion and auscultatory

palpation provide data far more reliable than roentgenographic records. *Technique:* 1. Adjust the stethoscope bell approximately at the centre of the organ to be outlined, thus permitting the bell to correspond to the hub of a wheel, and consider the periphery of the organ, or felloe of the wheel, to surround an area extending some distance from the bell, and beyond the margin of the organ under study. The spokes or radii lead from the hub outwards to the line transcribing the outer circle. 2. Begin percussion away from the bell (outside the organ under study) and continue directly along one radius. 3. Strike but a single stroke at one location on the chest. 4. Make percussion strokes of the same force, as change in note is most easily appreciated when percussion strokes are rhythmic. 5. Percuss along radii from different directions: mark each point where the percussion note changes, and thus rudely map out the organ in question. 6. Stroking of the skin and the use of the tuning fork while listening are delicate methods. The tuning fork while vibrating, is placed upon the surface of the body, advancing gradually toward the stethoscope bell, in the same manner as outlined for auscultatory percussion. It may be advantageously employed in the outlining of both solid and hollow viscera and in studying lesions of the lungs.—*Auscultatory Percussion and Palpation, L. Napoleon, Med. J. & Rec., October 15, 1924, cxx, 367.*—(*B. T. McM.*)

Symposium on Closed and Open Tuberculosis.—*E. Sergent:* The problem of closed tuberculosis is one of the most difficult in phthisiology. To deny the existence of closed tuberculosis is impossible; to give it too much importance is dangerous, as much from the doctrinal and scientific as from the practical viewpoint. Rist and Sergent have been among the foremost to lead a reaction against the diagnostic abuse of pulmonary tuberculosis. But, just as false tuberculosis encroaches on the list of the tuberculous, so is unrecognized or disregarded tuberculosis common. Theoretically, discrimination is easy, the only positive proof being the finding of the bacillus. But practically there may be much hesitancy. "Not to find bacilli does not mean they are not there. They may be rare, or only intermittently present." A careful search for bacilli in the stools of patients who do not spit will diminish the number of the "closed tuberculous." Likewise, before accepting a diagnosis of closed tuberculosis, one should make sure that no other affection is the cause of the symptoms, such as rhinopharyngeal affections, Basedow's disease, pulmonary syphilis, bronchiectasis. In the presence of hemoptysis, however, even though physical and roentgenographic findings be negative, the presumption is in favor of tuberculosis. These hemoptyses are due to little congestive reactions about latent tuberculous foci. In such cases the search for "indirect signs of localization," such as pain on pressure of the apex, supraclavicular adenitis, together with discrete stethoscopic signs, will confirm the diagnosis. Rist says, "bacilliferous expectoration being lacking, it is our duty to inquire seriously whether the signs and symptoms observed could not be explained by some other disease than tuberculosis. Only when no such other disease is found should the diagnosis of tuberculosis be tentatively made, as it were, by exclusion." This statement puts closed tuberculosis in its proper place. Thus, proof of closed tuberculosis demands prolonged and careful study. *F. Bezançon:* While in accord with the previous statements regarding the necessity for careful sputum examinations Bezançon considers it dangerous to think that the finding of tubercle bacilli is indispensable for the diagnosis. Tuberculous alveolitis is not often accompanied by elimination of bacilli; neither is tuberculous corticopleuritis. Abnormalities of the breath sounds, while not decisive, are far from being valueless. Functional symptoms, such as hemoptyses, fever without apparent cause, and persistent loss of weight, constitute a bundle of proofs of sufficient value on which to base a clinical diagnosis. Open tuberculosis is often preceded by a stage when there is no expectoration, or at least none containing bacilli. Doubtless Grancher's terminology cannot be strictly applied to the pathology of tuberculosis, but the facts observed by him are real. *M. G. Kuss:* The following four propositions are submitted: 1. In subjects affected by, or suspected of having, pulmonary tuberculosis, one ought to look for bacilli in the sputum with great perseverance by the best methods. It has also been clearly demonstrated that the best objective evidence of amelioration of the lesions is the diminution and disappearance of the bacilli in the sputum. 2. Tuberculosis patients may show bacillary sputum from the very beginning. 3. The abnormal breath sounds described by Grancher do not justify a diagnosis of tuberculosis. 4. Active closed pulmonary tuberculosis does not exist; it has no place in the nosography with the exception of the pleuritic forms. Of 1,000 cases so diagnosed Rist found that not one could be corroborated. With this last proposition, however, Kuss dissents. The study of the evolution of pulmonary tuberculosis and the anteced-

ent history is very instructive. There are often "revealing episodes," pulmonary or pleuropulmonary, which have sounded the alarm. These incidents should cause energetic and prolonged therapeutic measures to be taken to avoid future disasters. Rist fears diagnostic mistakes; one should rather fear the failure to recognize tuberculosis before it is too late for effective treatment. In the majority of cases the diagnosis of closed pulmonary tuberculosis, if made after a careful study, is correct, and is proved so in the course of several months or years. The period of uncertainty may be shortened by the therapeutic test and by the graduated diagnostic use of tuberculin. Even Rist does not eliminate all nonbacillary cases from the dispensary, but keeps them under observation as "nontuberculous." *L. Bernard:* Probably no one denies absolutely the existence of closed tuberculosis. It is really a question of proportion, and it is important to know whether cases of closed tuberculosis are common or rare, and what field of action the sanatorium and dispensary have. Cases of tuberculosis without bacilli may be separated into the following categories: 1. Open ulcerocavernous tuberculosis, with only intermittent bacillary elimination. 2. Ulcerocavernous pulmonary tuberculosis with persistently negative sputum. Even "silent cavities" may exist in such. A careful study of history nnd functional symptoms is here required to make the diagnosis. 3. Initial developing lesions. Here hemoptysis often occurs together with constitutional disturbances, and sometimes hematuria. The only physical signs may be roughened inspiration over an apex. In one case, two months later, a full-blown well marked pulmonary lesion was apparent. 4. Healed or apparently healed tuberculosis. 5. Inactive apical sclerosis of tuberculous nature, showing only anomalies of the vesicular murmur and no bacilli in the sputum. Grancher said that for such auscultatory signs to have real value they must be clearly defined, fixed and constant. Physicians too often obtain such signs with a normal radiological image. There may also be errors in interpretation of the hilar shadows in the adult as pathological, when they are within normal limits. Among the symptoms met with, hemoptysis is most characteristic, and if accompanied by a focus of râles near the apex or by localized hilar spots the diagnosis of tuberculosis may be made. After all, in the absence of a bacillary sputum only a tentative or probable diagnosis is generally justified. Animal inoculation of the sputum will enable a few more positive diagnoses to be made and should be performed oftener. *M. Burnand:* Of 119 patients treated at the popular sanatorium at Leysin in 1923, 79 were bacillary; and 40 nonbacillary. The latter consisted of (1) chronic catarrhal affections of the respiratory tract, 6 cases; (2) cervical adenitis, 1 case; (3) abortive or healed lesions, 5 cases; (4) pleural or pleurocortical tuberculosis, 6 cases; (5) diffuse fibrous lesions, apparently tuberculous, 4 cases; (6) acute or chronic miliary process, 5 cases; (7) early evolutive forms, 5 cases; (8) recent pneumothorax, 1 case; and (9) actual certain tuberculosis, demonstrated by previous findings of bacilli, by well-marked auscultatory signs (râles), or a subfebrile state with evident pulmonary lesions, 7 cases. One of them had an infiltrative laryngeal lesion, proved tuberculous by two biopsies. Burnand concludes that there are several forms of clinical thoracic tuberculosis not showing a bacillary sputum. Among these are the post-pleuritic beginning forms, corticopleuritis, the interstitial forms, the fibrous forms, the initial stages of the common fibrocaseous forms. Therefore, the reintroduction of methods based on a single pathognomonic sign, such as bacillary sputum seems a regrettable step backwards, as tuberculosis should when possible be treated before the appearance of bacillary expectoration. *P. F. Armand-Delille:* Rist is correct in stating that in the child affected with pulmonary tuberculosis, with few exceptions, one can obtain bacteriological proof of the disease if the bacilli are sought for, not in the sputum, which is rare, but in the stools; or better still in the stomach, either directly or by seeding Petroff's medium. The exceptional cases concern certain pulmonary consolidations which either clear up or do not break down and ulcerate for several years. In selecting children for the *Oeuvre Grancher* it is important to take those really indanger from parental infection, not from parents with doubtful disease. As Calmette has said, tuberculous contagion is largely a question of dose, and parents whose sputum is repeatedly negative are not dangerous. Then, as Bezançon insists, there is an initial exclusively lymphatic state characterized by tracheobronchial adenopathy, which may later be the point of departure for tuberculous generalization. This stage is recognized not by the finding of bacilli, but by physical signs, especially auscultation of the voice in the interscapular region. These positive signs are generally confirmed by radiography, and are indications for preventorium treatment with heliotherapy. *D'Espine* remarks especially on closed tuberculosis of children in the form of tracheobronchial adenopathy, diagnosed by auscultation of the voice at the level of the first three or four dorsal

vertebrae, and by the tuberculin skin reaction. This condition is a veritable sword of Damocles, which must be pointed out to the family in order that proper measures may be adopted to prevent later generalization. *Bard:* The scientific question of closed tuberculosis is settled, so that it is the practical clinical question of proportion and place which remains. Rist reproaches his contradictors for including among cases of closed tuberculosis a large number of nontuberculous, while they in turn reply that among a large series called by him nontuberculous a goodly number are likely, nevertheless, to be tuberculous. Neither side can prove its point conclusively. The practical side, however, pertains to military persons, popular sanatoria of limited capacity, antituberculosis work, and, tomorrow perhaps, social insurance. It is not so important to determine the number of subjects who do not expectorate bacilli but deserve the epithet, *tuberculous*, as it is to determine the number who are sick, or whose future is menaced, or who cannot work and deserve special care. Most authorities are agreed that the number of such subjects, whose sputum is persistently negative, is very small.—*Labesse, Jacquerod* and *Genevrier* also discussed the subject.—*Tuberculosis fermées et tuberculosis ouvertes, V^e Congrès Nat. d. l. Tuberc., reported in Rev. de la Tuberc., August, 1923, no. 4, 400.*—(*A. P.*)

Diagnosis of Early Pulmonary Tuberculosis.—The importance of certain factors in the history is emphasized. History of contact is especially important when it dates to childhood, and residence in an infected house is probably of as much significance as a positive family history. Pleurisy, especially with effusion, is usually tuberculous when primary. Loss of weight and strength is suggestive, and its gradual onset is especially so. The importance of cough has been over-estimated; its absence does not exclude tuberculosis. Prolonged cough is significant, however. Expectoration has about the same significance, but may mean more when present in the morning. "Catching cold readily" may be referable to causes other than tuberculosis. Occasionally indigestion is the presenting symptom. Afternoon fever, if prolonged, is strong presumptive evidence of active tuberculous disease, but in children may mean chronic purulent tonsillitis. A pulse accelerated out of proportion to temperature is very significant. Night sweats are usually a late symptom. Hemoptysis, if not of extrapulmonary origin, is usually pathognomonic. Physical examination should be carried out methodically. Inspection may reveal suggestive signs, such as unilateral scapular lagging. Palpation is of little value. Vocal fremitus is best tested with the ulnar edge of the hand. Percussion findings may be positive. With auscultation the detection of râles, with expiratory cough, over the apices is probably the earliest demonstrable sign of tuberculosis. Laboratory tests may show a secondary anemia and a fairly high lymphocyte percentage with a normal or slightly diminished white count. The Arneth count is not of great value. Thin purulent sputum is more likely to be tuberculous than the thick tenacious purulent type. The absence of tubercle bacilli has no bearing on the diagnosis, but their presence is pathognomonic. The basal metabolism test is useful in eliminating hyperthyroidism. A negative Pirquet test practically excludes the disease, while a positive one in childhood strongly suggests tuberculous infection. Roentgenography and fluoroscopy are of value, and stereoscopic photographs should be used in conjunction with physical findings. Prolonged observation, with a four-hourly temperature record, may be necessary to make a diagnosis. Apical lesions usually are tuberculous; basal ones generally are not. Râles, to be of definite significance, must be persistent, and moist râles are evidence of activity.—*The Diagnosis of Early Pulmonary Tuberculosis, W. E. Vest, West Virginia M. J., July, 1924, 1.*—(*J. B. A.*)

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